

# Sarah Bradley, Biology

---

University: University of Missouri-Columbia  
Year in School: Senior  
Hometown: Belton, Missouri  
Faculty Mentor: Dr. Martin K. Childers, Physical Medicine & Rehabilitation  
Funding Source: Life Sciences Undergraduate Research Opportunity Program

## **Investigating a possible treatment of Duchene Muscular Dystrophy with a novel calpain inhibitor**

Sarah E. Bradley, Jie Ning, Chad D. Markert, Daniel J. Bogan, Joe N. Kornegay, and Martin K. Childers

Duchene Muscular Dystrophy (DMD) is the most common lethal X-linked recessive muscle disease, affecting nearly one out of every 3,500 newborn males. Symptoms appear before age three and by eleven, most children are unable to walk. Few live past the age of 25. The genetic disorder is caused by a mutation in the dystrophin gene, eradicating the body's ability to produce the cytoskeletal protein, dystrophin. In normal muscle cells, dystrophin is part of a molecular complex that adds mechanical integrity to the sarcolemma by linking the cytoskeleton to the extracellular matrix. When the complex is disrupted, as in the case of DMD, the membrane is easily torn during regular muscle use. Damage to the membrane causes aberrant influxes of  $Ca^{++}$ , initiating a cascade of devastating molecular events in the sarcomere. Elevated  $Ca^{++}$  over activates a family of proteases known as calpains. Calpains cleave proteins at specific sites. Over-active calpains are thought to contribute to pathology in DMD. Compounds that hinder calpain activity present a possible treatment for the disease. A novel protease inhibitor has shown promising results in preliminary investigations in mice and this study was proposed to further explore the compound's effect on gene expression in canine muscle. An Affymetrix canine microarray was used to compare mRNA expression between normal dogs, dogs with golden retriever muscular dystrophy (GRMD), and inhibitor-treated GRMD dogs. By comparing these expression levels, we are able to speculate whether calpain inhibitor treatment is able to mitigate aberrant gene expression in GRMD dogs. Analysis of raw data is ongoing. Further study is required to determine if mRNA levels equate with the protein expression levels using PCR, Western Blotting, or other methods.